

REMARKS

Claims 1-13 are listed as pending in the application, which claims have been rejected.

Entry of the above amendments to the claims, and reconsideration and withdrawal of the rejections of claims 1-13 are requested.

DISCUSSION

Claims Renumbering

In the Office Action mailed February 15, 2005, the Examiner renumbered original claims 3-14 as claims 2-13 to account for the inadvertent omission of original claim 2. Applicants gratefully acknowledge such action which is reflected in the present numbering of the claims above.

Rejection of Claims 1-13 Under 35 U.S.C. §112

The Examiner rejected claims 1-13 under 35 U.S.C. §112, second paragraph, for incorporating the allegedly indefinite phrase "pharmaceutically acceptable derivative."

In response thereto, Applicants have amended relevant claims 1, 5-6, 8-9, and 11-12 by substituting the phrase "salt or solvate" for the word "derivative." Antecedent basis for such amendment is found in the instant description on page 3, lines 10-12.

Reconsideration and withdrawal of the rejection under 35 U.S.C. §112, second paragraph, is requested.

Rejection of Claims 7, 10, and 13 Under 35 U.S.C. §102

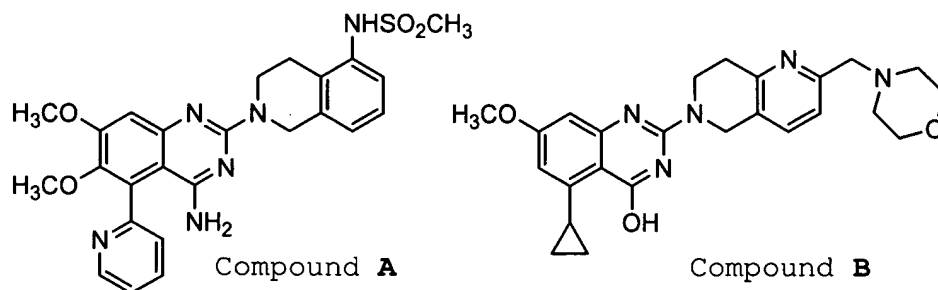
The Examiner rejected claims 7, 10, and 13 under 35 U.S.C. §102(b) in view of Scott, et al., (WO 99/11260; Scott,

et al., hereinafter) which teaches combinations of atorvastatin and  $\alpha_1$ -adrenergic receptor antagonists.

In response thereto, Applicants have canceled claims 7 and 10. Claim 13 has been amended in accordance with the traversals hereinbelow.

Rejection of Claims 8, 9, 11, and 12 Under 35 U.S.C. §103

The Examiner rejected claims 8, 9, 11, and 12 under 35 U.S.C. §103(a) as being unpatentable over Scott, et al., in view of Davis, et al. (U.S. Pat. Appl'n. Pub. No. 2003/0133978; Davis, et al., hereinafter), and Blagg, et al. (U.S. Pat. Appl'n. Pub. No. 2004/0029859; Blagg, et al., hereinafter). The Examiner alleged that Scott, et al., in combination with Davis, et al., and Blagg, et al., which teach, respectively, 4-amino-6,7-dimethoxy-2-(5-methanesulfonamido-1,2,3,4-tetrahydroisoquinol-2-yl)-5-(2-pyridyl)quinazoline (Compound A) and 5-cyclopropyl-7-methoxy-2-(2-morpholin-4-ylmethyl-7,8-dihydro[1,6]-naphthyridin-6(5H)-yl)-4(3H)-quinazolinone (Compound B), renders the claimed combination compositions obvious.



In response thereto, Applicants submit that neither Davis, et al., nor Blagg, et al., is a proper reference against the instant application.

Section 103(c) of 35 U.S.C. provides that "[s]ubject matter developed by another person, which qualifies as prior

art only under one or more of subsections (e), (f), and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person."

Statement of Common Ownership

Davis, et al., which claims priority to U.S. Provisional Appl'n. Serial No. 60/340,717 through U.S. Serial No. 10/269,551, and the instant application, U.S. Serial No. 10/663,082, were, at the time the present invention was made, under an obligation of assignment to Pfizer Inc. In support thereof, Applicants refer to the Assignments recorded at Reel 012717, Frame 0168, and Reel 012717, Frame 0056, copies of which are transmitted concurrently herewith for the Examiner's consideration, and marked collectively as "EXHIBIT A."

Blagg, et al., which claims priority to U.S. Provisional Appl'n. Serial No. 60/374,894, through U.S. Serial No. 10/387,106, and the instant application were, at the time the present invention was made, also under an obligation of assignment to Pfizer Inc. In support thereof, Applicants refer to the Assignments recorded at Reel 012980, Frame 0794, and Reel 012971, Frame 0067, copies of which are transmitted concurrently herewith for the Examiner's consideration, and marked collectively as "EXHIBIT B."

In view of the foregoing, reconsideration and withdrawal of the rejection of claims 8, 9, 11, and 12 under 35 U.S.C. §103(a) are requested.

Rejection of Claims 1-6 Under 35 U.S.C. §103

The Examiner rejected claims 1-6 under 35 U.S.C. §103(a) as being unpatentable over Weisman, et al. (U.S. Pat. Appl'n. Pub. No. 2002/0004521; Weisman, et al., hereinafter) and Thompson, et al. (U.S. Pat. No. 6,177,430; Thompson, et al., hereinafter), in view of Scott, et al., Lawyer, et al. (U.S. Pat. No. 6,423,719; Lawyer, et al., hereinafter), Davis, et al., and Blagg, et al. The Examiner alleged, in sum, that it was *prima facie* obvious to employ a combination of an HMG-CoA reductase inhibitor and an  $\alpha_1$ -adrenergic receptor antagonist to treat BPH, in view of the teachings of Weisman, et al., (treatment of BPH with an HMG-CoA reductase inhibitor) and Thompson, et al., (treatment of BPH with an  $\alpha_1$ -adrenergic receptor antagonist) with the reasonable expectation of producing an additive effect.

In response thereto, Applicants have amended the present method claims by canceling claim 4 and the agents terazosin, doxazosin, prazosin, bunazosin, alfuzosin, naftopidil, tamsulosin, and silodosin from claim 3. The remaining compound limitations of claim 3 have been incorporated into claim 1. Accordingly, any continued basis for the standing rejection must now be derived from the now disqualified Davis, et al., and Blagg, et al., references, which disclose Compounds **A** and **B**, hereinabove. As stated in the instant description on page 9, lines 20-26, it is Applicant's belief that the claimed combinations will exhibit synergistic utility in the treatment of benign prostatic hyperplasia (BPH). In confirmation of such assertion, Applicants submit concurrently herewith for the Examiner's consideration a document entitled "SYNERGISTIC COMBINATION STUDY", denoted as "EXHIBIT C", the contents of which demonstrate the synergistic utility of a combination of

Compound **A** and atorvastatin in treating BPH. In view of the close structural similarity to Compound **A**, Applicants posit that Compound **B** will also exhibit similar synergistic utility in combination with atorvastatin. Applicants have further amended instant method claim 1, and composition claims 8-9, and 11-12 to incorporate synergistic limitations thereinto.

Reconsideration and withdrawal of the rejection of claims 1-6 under 35 U.S.C. §103(a) are requested.

A prompt and favorable action on the merits is respectfully solicited.

Respectfully submitted,

Date: May 16, 2005



Carl J. Goddard  
Attorney for Applicants  
Reg. No. 39,203  
Tel.: (860) 441-4902

PFIZER INC  
Patent Department, MS 8260-1611  
Eastern Point Road  
Groton, CT 06340  
(860) 441-4902

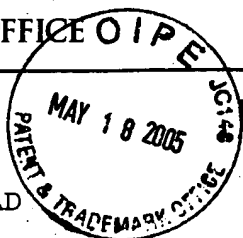


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# EXHIBIT A

MAY 21, 2002

PFIZER INC.  
GREGG C. BENSON  
EASTERN POINT ROAD  
MS 4159  
GROTON, CT 06340



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Chief Information Officer  
Washington, DC 20231  
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RECORDATION DATE: 03/13/2002

REEL/FRAME: 012717/0168  
NUMBER OF PAGES: 3

BRIEF: ASSIGNMENT OF ASSIGNOR'S INTEREST (SEE DOCUMENT FOR DETAILS).

ASSIGNOR:  
MACRAE, ROSS JAMES

DOC DATE: 02/18/2002

ASSIGNOR:  
SMITH, JANET SARAH

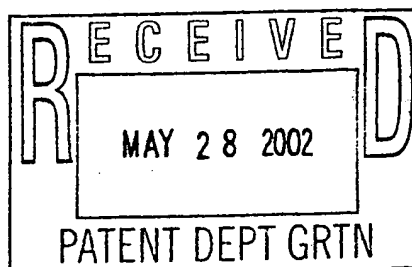
DOC DATE: 02/18/2002

ASSIGNEE:  
PFIZER LIMITED  
RAMSGATE ROAD  
SANDWICH KENT, ENGLAND CT13 9NJ

SERIAL NUMBER: 60340717  
PATENT NUMBER:

FILING DATE: 10/30/2001  
ISSUE DATE:

THERESA FREDERICK, EXAMINER  
ASSIGNMENT DIVISION  
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*Kam*

03-29-2002


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## 1. Name of conveying party(ies):

 Ross James MacRae  
 Janet Sarah Smith

3-13-02

 Additional name(s) of conveying party(ies) attached? ☐ Yes ☐ No

## 2. Name and address of receiving party(ies):

Name: Pfizer Limited.Street Address: Ramsgate RoadCity: Sandwich, Kent State: England Zip: CT13 9NJ

## 3. Nature of conveyance:

☒ Assignment ☐ Merger  
☐ Security Agreement ☐ Change of Name  
☐ Other \_\_\_\_\_

 Additional name(s) & address(es) attached? ☐ Yes ☒ No
Execution Date: February 18, 2002

## 4. Application number(s) or patent number(s):

If this document is being filed together with a new application, the execution date of the application is

A. Patent Application No.(s)

B. Patent No. (s)

60/340,717
 Additional numbers attached? ☐ Yes ☒ No

## 5. Name and address of party to whom correspondence concerning document should be mailed:

Name: Gregg C. BensonInternal Address: Pfizer Inc.Street Address: Eastern Point Road, MS 4159City: Groton State: Connecticut ZIP: 06340

## 6. Total number of pages including cover sheet, attachments and document: 3

7. Total fee (37 CFR 3.41).....\$ 40.00☐ Enclosed☒ Authorized to be charged to deposit account

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Todd M. Crissey (Reg. No. 37,807)

Name of Person Signing

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03/28/2002 DBYRNE 00000206 161445 60340717

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na/10964Assignment1.doc

ASSIGNMENT

For valuable consideration, the receipt and adequacy of which is hereby acknowledged, we, **Ross James MACRAE** and **Janet Sarah SMITH**, of Pfizer Global Research and Development, Ramsgate Road, Sandwich, Kent CT13 9NJ, England, respectively, hereby sell, assign and transfer unto PFIZER LIMITED, a corporation organized and existing under the laws of England, and having a place of business at Ramsgate Road, Sandwich, Kent, CT13 9NJ, United Kingdom, our entire right, title and interest, in all countries of the world, in and to United Kingdom Patent Application No. **0124455.7**, filed **11<sup>th</sup> October 2001**, entitled **Pharmaceutical Formulations**, and having Pfizer Docket No. **PCS10964GML-PROV**; our entire right, title and interest, in all countries of the world, in and to United States Provisional Patent Application Serial No. **60/340,717**, filed **30<sup>th</sup> October 2001**, entitled as above, and having Pfizer Docket No. **PC10964**; our entire right, title and interest, in all countries of the world, in and to all our inventions, both joint and sole, disclosed in said United Kingdom Patent Application and said United States Provisional Patent Application; our entire right, title and interest in and to all applications, filed in any country of the world, for Letters Patent for any or all of said inventions, and any and all Letters Patent granted thereon; and the right to claim priority from either or both of said United Kingdom Patent Application and said United States Provisional Patent Application under the Paris Convention for the Protection of Industrial Property, and under any other such treaties which afford similar priority-claiming privileges;

and we hereby agree, whenever requested, to communicate to PFIZER LIMITED, its successors and assigns, any and all facts known to us respecting said inventions; to testify in any legal proceedings respecting said inventions; and to execute any and all papers deemed necessary and proper by PFIZER LIMITED, its successors and assigns, to obtain and maintain proper patent protection on said inventions, in all countries of the world.

Signed and witnessed this 18<sup>th</sup> day of February 2002  
at Sandwich, Kent, England

Ross James Macrae  
(Inventor) **Ross James Macrae**

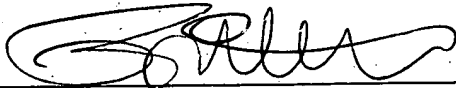
In the presence of:

L.P. Kendall  
**L.P. Kendall**  
(Typed or printed name of witness)



Signed and witnessed this 18th day of February 2002

At Sandwich, Kent, England



(Inventor) Janet Sarah Smith

In the presence of:



L.P. Kendall

(Typed or printed name of witness)



10964

MAY 21, 2002

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Washington, DC 20231  
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RECORDATION DATE: 03/13/2002

REEL/FRAME: 012717/0056  
NUMBER OF PAGES: 2

BRIEF: ASSIGNMENT OF ASSIGNOR'S INTEREST (SEE DOCUMENT FOR DETAILS).

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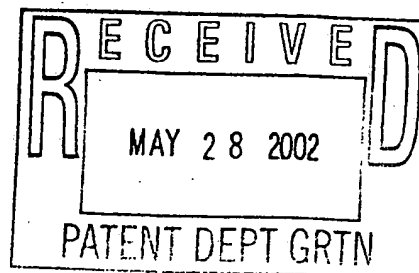
DOC DATE: 02/20/2002

ASSIGNEE:  
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235 EAST 42ND STREET  
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SERIAL NUMBER: 60340717  
PATENT NUMBER:

FILING DATE: 10/30/2001  
ISSUE DATE:

DOROTHY RILEY, EXAMINER  
ASSIGNMENT DIVISION  
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03-29-2002


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☐ Security Agreement ☐ Change of Name  
☐ Other \_\_\_\_\_
Execution Date: February 20, 2002

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 Name: Pfizer Inc.  
 Street Address: 235 East 42nd Street, 20th Floor  
 City: New York State: New York Zip: 10017-5755

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4. Application number(s) or patent number(s):

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A. Patent Application No.(s) B. Patent No. (s)

60/340,717
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Name: Gregg C. BensonInternal Address: Pfizer Inc.Street Address: Eastern Point Road, MS 4159City: Groton State: Connecticut ZIP: 06340
 6. Total number of pages including cover sheet  
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7. Total fee (37 CFR 3.41).....\$ 40.00☐ Enclosed☒ Authorized to be charged to deposit account

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Todd M. Crissey (Reg. No. 37,807)

Name of Person Signing

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ASSIGNMENT

For valuable consideration, the receipt and adequacy of which is hereby acknowledged, PFIZER LIMITED, a corporation organized and existing under the laws of England, and having a place of business at Ramsgate Road, Sandwich, Kent, CT13 9NJ, United Kingdom, hereby sells, assigns and transfers unto PFIZER INC., a corporation organized and existing under the laws of the State of Delaware, United States of America, and having a place of business at 235 East 42nd Street, New York, New York 10017, United States of America, its entire right, title and interest, in all countries of the world except the United Kingdom, in and to United Kingdom Patent Application No. 0124455.7, filed 11<sup>th</sup> October 2001, entitled **Pharmaceutical Formulations**, and having Pfizer Docket No. PCS10964GML-PROV; its entire right, title and interest, in all countries of the world except the United Kingdom, in and to United States Provisional Patent Application Serial No. 60/340,717, filed 30<sup>th</sup> October 2001, entitled as above, and having Pfizer Docket No. PC10964; its entire right, title and interest in all countries of the world except the United Kingdom, in and to all the inventions disclosed in said United Kingdom Patent Application and said United States Provisional Patent Application; and its entire right, title and interest in and to all applications filed in all countries of the world except the United Kingdom for Letters Patent for any and all of said inventions; and its entire right, title and interest in and to all Letters Patent granted in all countries of the world except the United Kingdom on the foregoing applications;

and PFIZER LIMITED hereby agrees, whenever requested, to communicate to PFIZER INC., its successors and assigns, any and all facts known to it respecting said inventions; to testify in any legal proceedings respecting said inventions; and to execute any and all papers deemed necessary and proper by PFIZER INC., its successors and assigns, to obtain and maintain proper patent protection on said inventions, in all countries of the world.

PFIZER LIMITED

Date: 20th February 2002

by:

D. J. Wood  
David John Wood  
Authorized Attorney  
of Pfizer Limited

In the presence of:

L. P. Kendall

L. P. Kendall  
(Typed or printed name of witness)



UNITED STATES  
PATENT AND  
TRADEMARK OFFICE

# EXHIBIT B

AUGUST 14, 2002

PFIZER INC.  
GREGG C. BENSON  
EASTERN POINT ROAD, MS 4159  
GROTON, CONNECTICUT 06340



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RECORDATION DATE: 06/11/2002

REEL/FRAME: 012980/0794  
NUMBER OF PAGES: 4

BRIEF: ASSIGNMENT OF ASSIGNOR'S INTEREST (SEE DOCUMENT FOR DETAILS).

ASSIGNOR:  
BLAGG, JULIAN

DOC DATE: 05/20/2002

ASSIGNOR:  
FRAY, MICHAEL JONATHAN

DOC DATE: 05/20/2002

ASSIGNOR:  
LEWIS, MARK LLEWELLYN

DOC DATE: 05/20/2002

ASSIGNOR:  
MATHIAS, JOHN PAUL

DOC DATE: 05/20/2002

ASSIGNOR:  
STEFANIAK, MARK HENRYK

DOC DATE: 05/20/2002

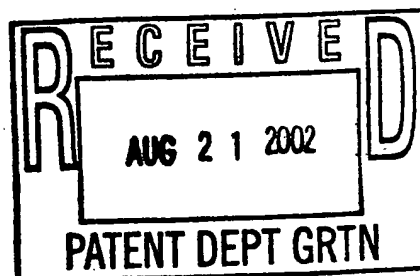
ASSIGNOR:  
STOBIE, ALAN

DOC DATE: 05/20/2002

ASSIGNEE:  
PFIZER LIMITED  
RAMSGATE ROAD  
SANDWICH, KENT, ENGLAND CT13 9NJ

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*Kam*



012980/0794 PAGE 2

SERIAL NUMBER: 60374894  
PATENT NUMBER:

FILING DATE: 04/23/2002  
ISSUE DATE:

ALLYSON PURNELL, EXAMINER  
ASSIGNMENT DIVISION  
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102121184

original documents or copy thereon.

To the Assistant Commissioner (if applicable)

## 1. Name of conveying party(ies):

Julian Blagg  
Michael Jonathan Fray  
Mark Llewellyn Lewis  
John Paul Mathies  
Mark Henryk Stefaniak  
Alan Stobie

6-11-02

Additional name(s) of conveying party(ies) attached? ☐ Yes ☐ No

## 3. Nature of conveyance:

- ☒ Assignment ☐ Merger  
☐ Security Agreement ☐ Change of Name  
☐ Other \_\_\_\_\_

Execution Date: May 20, 2002

## 2. Name and address of receiving party(ies):

Name: Pfizer Limited  
Street Address: Ramsgate Road  
City: Sandwich, Kent State: England Zip: CT13 9NJ

Additional name(s) & address(es) attached? ☐ Yes ☒ No

## 4. Application number(s) or patent number(s):

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60/374,894Additional numbers attached? ☐ Yes ☒ No

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## 6. Total number of pages including cover sheet, attachments and document: 3

7. Total fee (37 CFR 3.41).....\$ 40.00

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Julian Hlapp  
Michael Jonathan Fray  
Mark Llewellyn Lewis  
John Paul Mathias  
Mark Henryk Stefanlak  
Alan Stoble

6-11-02

Additional name(s) of conveying party(ies) attached? ☐ Yes ☐ No

## 3. Nature of conveyance:

- ☒ Assignment ☐ Merger  
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☐ Other \_\_\_\_\_

Execution Date: May 20, 2002

## 2. Name and address of receiving party(ies):

Name: Pfizer Limited  
Street Address: Ramsgate Road  
City: Sandwich, Kent State: England Zip: CT13 9NJAdditional name(s) & address(es) attached? ☐ Yes ☒ No

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A. Patent Application No.(s)

B. Patent No. (s)

60/374,894Additional numbers attached? ☐ Yes ☒ No

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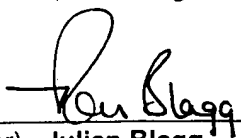


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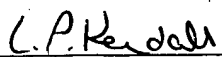
For valuable consideration, the receipt and adequacy of which is hereby acknowledged, we, **Julian BLAGG, Michael Jonathan FRAY, Mark Llewellyn LEWIS, John Paul MATHIAS, Mark Henryk STEFANIAK and Alan STOBIE**, of Pfizer Global Research and Development, Ramsgate Road, Sandwich, Kent CT13 9NJ, England, respectively, hereby sell, assign and transfer unto PFIZER LIMITED, a corporation organized and existing under the laws of England, and having a place of business at Ramsgate Road, Sandwich, Kent, CT13 9NJ, United Kingdom, our entire right, title and interest, in all countries of the world, in and to United Kingdom Patent Application No. **0206033.3**, filed **14<sup>th</sup> March 2002**, entitled **Compounds Useful In Therapy**, and having Pfizer Docket No. **PCS22026SMC-PROV**; our entire right, title and interest, in all countries of the world, in and to United States Provisional Patent Application, Serial No. **60/374,894**, filed **23<sup>rd</sup> April 2002**, entitled as above, and having Pfizer Docket No. **PCS22026**; our entire right, title and interest, in all countries of the world, in and to all our inventions, both joint and sole, disclosed in said United Kingdom Patent Application and said United States Provisional Patent Application; our entire right, title and interest in and to all applications, filed in any country of the world, for Letters Patent for any or all of said inventions, and any and all Letters Patent granted thereon; and the right to claim priority from either or both of said United Kingdom Patent Application and said United States Provisional Patent Application under the Paris Convention for the Protection of Industrial Property, and under any other such treaties which afford similar priority-claiming privileges;

and we hereby agree, whenever requested, to communicate to PFIZER LIMITED, its successors and assigns, any and all facts known to us respecting said inventions; to testify in any legal proceedings respecting said inventions; and to execute any and all papers deemed necessary and proper by PFIZER LIMITED, its successors and assigns, to obtain and maintain proper patent protection on said inventions, in all countries of the world.

Signed and witnessed this 20<sup>th</sup> day of May 2002  
at Sandwich, Kent, England

  
\_\_\_\_\_  
(Inventor) **Julian Blagg**

In the presence of:

  
\_\_\_\_\_  
**L.P. Kendall**  
(Typed or printed name of witness)

Signed and witnessed this 20th day of May 2002

At Sandwich, Kent, England

Michael Jonathan Fray  
(Inventor) **Michael Jonathan Fray**

In the presence of:

L.P. Kendall  
L.P. Kendall  
(Typed or printed name of witness)

Signed and witnessed this 20th day of May 2002

At Sandwich, Kent, England

Mark Llewellyn Lewis  
(Inventor) **Mark Llewellyn Lewis**

In the presence of:

L.P. Kendall  
L.P. Kendall  
(Typed or printed name of witness)

Signed and witnessed this 20th day of May 2002

At Sandwich, Kent, England

John Paul Mathias  
(Inventor) **John Paul Mathias**

In the presence of:

L.P. Kendall  
L.P. Kendall  
(Typed or printed name of witness)

Signed and witnessed this 20<sup>th</sup> day of May 2002

At Sandwich, Kent, England

Mark Henryk Stefaniak  
(Inventor) Mark Henryk Stefaniak

In the presence of:

L.P. Kendall

L.P. Kendall  
(Typed or printed name of witness)

Signed and witnessed this 20<sup>th</sup> day of May 2002

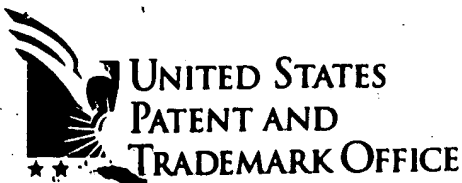
At Sandwich, Kent, England

[Signature]  
(Inventor) Alan Stobie

In the presence of:

L.P. Kendall

L.P. Kendall  
(Typed or printed name of witness)



AUGUST 12, 2002

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Chief Information Officer  
Washington, DC 20231  
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GREGG C. BENSON  
EASTERN POINT ROAD, MS 4159  
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DOC DATE: 05/21/2002

ASSIGNEE:  
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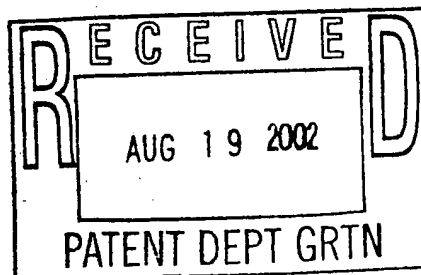
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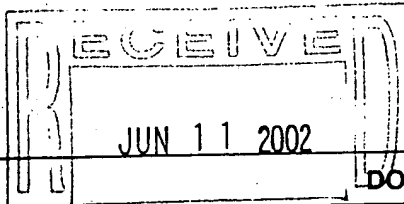
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and PFIZER LIMITED hereby agrees, whenever requested, to communicate to PFIZER INC., its successors and assigns, any and all facts known to it respecting said inventions; to testify in any legal proceedings respecting said inventions; and to execute any and all papers deemed necessary and proper by PFIZER INC., its successors and assigns, to obtain and maintain proper patent protection on said inventions, in all countries of the world.

PFIZER LIMITED

Date: 21st May 2002

by: D.J. Wood  
David John Wood  
Authorized Attorney  
of Pfizer Limited

In the presence of:

L.P. Kendall

L.P. Kendall  
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B. Patent No. (s)

60/374,894Additional numbers attached? ☐ Yes ☒ No5. Name and address of party to whom  
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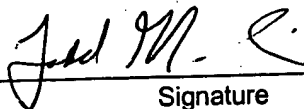
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# EXHIBIT C

## SYNERGISTIC COMBINATION STUDY

### Study Outline

In order to confirm the synergistic therapeutic effect of a combination of atorvastatin and an  $\alpha_1$ -adrenergic receptor antagonist in the treatment of benign prostatic hyperplasia (BPH), a 12-week study in men with symptomatic BPH was conducted. An IPSS (International Prostate Symptom Score; M. J. Barry, et al., Journal of Urology, 164, 1559-1564 (2000)) was recorded at baseline, during, and at the conclusion of a double-blind treatment regimen. The IPSS was composed of seven questions relating to frequency and quality of micturation (urination). The respondent's answers were graded from 0-5 on a Likert scale. The higher the Score, the more severe the reported lower urinary tract symptom(s). The primary endpoint was mean change in Score from baseline to end of study in the intent-to-treat population. In this study, the  $\alpha_1$ -adrenergic receptor antagonist 4-amino-6,7-dimethoxy-2-(5-methanesulfonamido-1,2,3,4-tetrahydroisoquinol-2-yl)-5(2-pyridyl)quinazoline was used. There were four treatment groups: 1 mg, 3 mg, and 6 mg  $\alpha_1$ -adrenergic receptor antagonist, and placebo.

### Effect of Atorvastatin Treatment Alone

In order to determine the efficacy of atorvastatin treatment alone, a 26-week study was conducted comparing the effects of atorvastatin administration on lower urinary tract symptoms in men with symptomatic BPH. As before, the primary endpoint was mean change in IPSS from baseline to the end of the study in the intent-to-treat population. The IPSS was recorded at baseline, during, and at the end of double-blind treatment.

Table 1

Mean change in IPSS from Baseline to Week 26

Atorvastatin dosage	13 Weeks	26 Weeks
80 mg	+0.1	-0.2



As is evidenced from the study results shown in Table 1 above, no significant improvement in Scores was observed by the administration of atorvastatin alone over a treatment duration of 26 weeks.

#### Combination Treatment Results

Efficacy in subjects receiving atorvastatin and  $\alpha_1$ -adrenergic receptor antagonist therapy was then compared with efficacy in subjects who were receiving  $\alpha_1$ -adrenergic receptor antagonist therapy alone. This comparison demonstrated that, for each dose group of  $\alpha_1$ -adrenergic receptor antagonist, synergistic efficacy was seen in the atorvastatin-treated group vs. the atorvastatin-untreated group, when compared with the placebo response in each group.

Table 2

Mean change in IPSS from Baseline to Week 12

$\alpha_1$ -Adrenergic receptor antagonist dosage group	$\alpha_1$ -Adrenergic receptor antagonist without atorvastatin	$\alpha_1$ -Adrenergic receptor antagonist combination with atorvastatin
1 mg	-1.3	-6.4
3 mg	-2.5	-4.0
6 mg	-2.1	-15.7

#### Conclusion

Based upon the results of the administration of atorvastatin alone, a treatment Score essentially equivalent to that observed for the administration of the  $\alpha_1$ -adrenergic receptor antagonist alone would have been expected if the effect of the combination atorvastatin/ $\alpha_1$ -adrenergic receptor antagonist treatment had been merely additive. That improvements in Scores of approximately 5 times that expected for an additive effect in the 1 mg treatment group and 7.5 times that expected for the 6 mg treatment group were observed is indicative of a

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Art Unit 1614

direct synergistic effect resulting from administration of a combination of atorvastatin and an  $\alpha_1$ -adrenergic receptor antagonist.